Neurobehavioral And Oxidative Stress Alterations Following Methylmercury And Retinyl Palmitate Co-Administration In Pregnant And Lactating Rats And Their Offspring

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Abstract

Fish consumption and ubiquitous methylmercury (MeHg) exposure represent a public health problem globally. Micronutrients presented in fish affects MeHg uptake/distribution. Vitamin A (VitA), another fish micronutrient is used in nutritional supplementation, especially during pregnancy. However, there is no information about the health effects arising from their combined exposure. The present study aimed to examine the effects of both MeHg and retinyl palmitate administered to pregnant and lactating rats. Thirty Wistar female rats were orally supplemented with MeHg (0,5 mg/Kg/day) and retinyl palmitate (7500 µg RAE[1]/Kg/day), either individually or in combination from the gestational day 0 to weaning. In dams, maternal behavior was scored. In neonatal and infant offspring, associative learning and neurodevelopment were evaluated. Further periadolescent male and female pups were assessed for open field, habituation and object recognition using episodic-like memory paradigm. Maternal and offspring redox parameters were evaluated. Our results showed no effects of MeHg-VitA co-administration in the quality of maternal care but showed subtle alterations in the pro-oxidant response of the hippocampus. In offspring, MeHg-VitA co-exposure affected early associative learning in neonatal pups, with no further modifications in neurodevelopment, and no locomotor or exploratory alterations in later developmental stages. Habituation was altered in a sex-dependent manner, but no overall memory disturbances were encountered. Finally, MeHg-VitA co-administration reduced lipoperoxidation in male offspring hippocampus. In conclusion, VitA co-administration in dams, under our exposure protocol, can counteract the deleterious neurodevelopmental effects solely attributed to low-dose MeHg in a tissue-specific mechanism, suggesting a protective effect of VitA against MeHg-induced oxidative damage in the central nervous system, especially in the offspring. Further work is needed to confirm our findings and elucidate the molecular mechanisms of MeHg-VitA modulation. Pre-clinical assays are

necessary to demonstrate the potential therapeutical use of VitA in populations directly or indirectly exposed to MeHg..

Keywords

Behavior; Co-Exposure; Methylmercury; Oxidative Stress; Pregnancy; Retinyl palmitate.